EX-2

EXHIBIT 2

NDA APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-130

OCT 9 1996

Parke-Davis Pharmaceutical Research
Attention: Ms. Mary Taylor
Director, Worldwide Regulatory Affairs
2800 Plymouth Road, P.O. Box 1047
Ann Arbor, MI 48106-1047

Dear Ms. Taylor:

Please refer to your December 27, 1990, new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Estrostep -21 (norethindrone acetate and ethinyl estradiol) Tablets and Estrostep-Fe (norethindrone acetate and ethinyl estradiol tablets and ferrous fumarate) Tablets.

We acknowledge receipt of your amendments dated April 9, May 24, July 17, September 23, and October 2, 3, and 8 (telefacsimile), 1996, in response to our not approvable letter dated August 27, 1992.

This new drug application provides for the prevention of pregnancy.

We have completed the review of this application, including the submitted draft labeling, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the draft labeling in the submission dated September 23 (blister, cartons, and pouch), and October 3, 1996 (prescribing information and patient information). Accordingly, the application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the draft labeling submitted on September 23 (blister, cartons, and pouch), and October 3, 1996 (prescribing information and patient information). Marketing the product with FPL that is not identical to this draft labeling may render the product misbranded and an unapproved new drug.

Please submit sixteen copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes this submission should be designated "FINAL PRINTED LABELING" for approved NDA 20-130. Approval of this submission by FDA is not required before the labeling is used.

Should additional information relating to the safety and effectiveness of the drug become available, revision of that labeling may be required.

We remind you of your Phase 4 commitments specified in your submission dated April 9, 1996. These commitments, along with any completion dates agreed upon, are listed below. Protocols, data, and final reports should be submitted to your IND for this product and a copy of the cover letter sent to this

NDA. Should an IND not be required to meet your Phase 4 commitments, please submit protocol, data, and final reports to this NDA as correspondences. For administrative purposes, all submissions, including labeling supplements, relating to these Phase 4 commitments must be clearly designated "Phase 4 Commitments." These commitments are as follows:

1. To conduct a multiple dose biopharmaceutics study designed to address the deficiencies discussed with the Division of Biopharmaceutics. You also agreed to submit the protocol within 30 days after approval. The study should be completed within one-year following your receipt of the Agency's comments on the protocol. The study should use the marketed tablets and should incorporate dosing regimens of the product consistent with its labeling.

2. To update the **CLINICAL PHARMACOLOGY** section of the labeling using data from the above study (bioavailability and pharmacokinetics values) and other relevant information (metabolism and excretion) upon completion of the above study.

3. To submit additional dissolution profiles for three production lots of each strength of Estrostep Tablets (1/20, 1/30, and 1/35 NA/EE) using the new official USP method within the next six months.

In addition, please submit three copies of the introductory promotional material that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division and two copies of both the promotional material and the package insert directly to:

Food and Drug Administration
Division of Drug Marketing, Advertising and Communications,
HFD-40
5600 Fishers Lane
Rockville, Maryland 20857

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

Please submit one market package of the drug when it is available.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

Should you have any questions, please contact Ms. Christina Kish at (301) 827-4260

Sincerely yours,

Lisa Rarick, M.D.
Director
Division of Reproductive and Urologic
Drug Products (HFD-580)
Office Of Drug Evaluation II
Center for Drug Evaluation and Research